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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/551,550	06/29/2006	Masayuki Tanaka	Q90646	3838

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EXAMINER	
RAGHU, GANAPATHIRAM	
ART UNIT	**PAPER NUMBER**
1652	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/551,550	TANAKA ET AL.	
	Examiner	Art Unit	
	GANAPATHIRAMA RAGHU	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 April 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-21* is/are pending in the application.

4a) Of the above claim(s) *9-15 and 18-21* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8,16 and 17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *29 June 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *09/30/2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☒ Other: *SEQALIGN*.

Detailed Action

Claims 1-21 are pending in this application for examination. Claims 1-8, 16 and 17 are now under consideration. Claims 9-15 and 18-21 remains withdrawn as they are drawn to non-elected inventions.

Election/Restrictions

Applicant's election of Group I, claims 1-8, 16 and 17 and as a species "Chondroitin sulfate D" without traverse for prosecution with the proviso that the applicants' reserve the right to file a Divisional Application to non-elected claims, in the reply filed on 04/18/2008 is acknowledged. Examiner acknowledges and thanks the applicant for bringing to the notice of the preliminary amendment of claims dated 09/30/05. Examiner for the record would like to reiterate the groupings of the non-elected inventions are as follows:

Group II: Claims 9-12, drawn to a method of specifically cleaving one sugar chain or two or more sugar chains and to a method of producing sugar chains having a decreased molecular weight selected from the group consisting of hyaluronic acid, chondroitin sulfate A, chondroitin sulfate C and chondroitin sulfate D which comprises reacting with a polypeptide comprising the sequence of SEQ ID NO: 2.

Group III: Claims 13-15, drawn to a method of producing a catalyst or medicament, wherein said method comprises expressing a protein using a DNA that encodes a polypeptide comprising the sequence of SEQ ID NO: 2 and has the activity of specifically cleaving one sugar chain or two or more sugar chains and to a method of producing sugar chains having a decreased molecular weight selected from the group consisting of hyaluronic acid, chondroitin sulfate A, chondroitin sulfate C and chondroitin sulfate D.

Group IV: Claims 18-21, drawn to a method of treating a disease in which one sugar chain or two or more sugar chains selected from the group consisting of hyaluronic acid, chondroitin sulfate A, chondroitin sulfate C and chondroitin sulfate D is/are excessively present in the body tissue, said method comprises administering the elected polypeptide of group I.

Priority

Acknowledgment is made of applicant's claim for foreign priority under 35 U.S.C. 119(a)-(d). This application is a 371 of PCT/JP04/04695 filed on 03/31/2004 and claims the priority dates of Japanese applications 2003-97301 filed on 03/31/2003 and 2003-113965 filed on 04/18/2003. Examiner notes that the certified copies of the applications dated 09/30/2005 are provided. However, English translations for the said Japanese applications are not provided.

Information Disclosure Statement

The information disclosure statement (IDS) submitted on 09/30/2005 is in compliance with the provisions of 37 CFR 1.97. Accordingly, examiner has considered the information disclosure statement.

Claim Rejections: 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1 (claim 2 depending therefrom), 3 (claim 4 depending therefrom) and 5 (claims 6-8 depending therefrom) are rejected under 35 U.S.C. 101, because the claim reads on non-statutory subject matter. Claims 1, 3 and 5 are drawn to 'A catalyst…', 'A cleavage agent…' and 'A medicament…' respectively which reads on the product of nature. Claims directed to such subject matter are considered non-statutory because they read on products of nature. Examiner

suggests amending the claim to recite 'An isolated catalyst…', 'An isolated cleavage agent…' and 'An isolated medicament…' to show the hand of man, in order to overcome the rejection.

Claim Rejections: 35 USC § 112-First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Enablement

Claims 1-8, 16 and 17 are rejected under 35 U.S.C. 112, first paragraph, because the specification is being enabling for an isolated catalyst or an isolated cleavage agent specifically cleaving one sugar chain or two or more sugar chains selected from the group consisting of hyaluronic acid, chondroitin sulfate A, C and D, said catalyst or cleavage agent is a protein comprising the amino acid sequence of SEQ ID NO: 2, composition (medicament) and fusion protein comprising said protein, does not reasonably provide enablement for any catalyst or any cleavage agent specifically cleaving one sugar chain or two or more sugar chains selected from the group consisting of hyaluronic acid, chondroitin sulfate A, C and D, said catalyst or cleavage agent is a protein comprising an amino acid sequence of SEQ ID NO: 2, wherein one or several amino acid residues are deleted, substituted, inserted and/or transposed and further compositions (medicaments) and fusion proteins comprising said proteins. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and or use the invention commensurate in scope with the claim.

Factors to be considered in determining whether undue experimentation is required are summarized in *In re Wands* (858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)) as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3)

the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claim(s).

Claims 1-8, 16 and 17 are so broad as to encompass any catalyst or any cleavage agent specifically cleaving one sugar chain or two or more sugar chains selected from the group consisting of hyaluronic acid, chondroitin sulfate A, C and D, said catalyst or cleavage agent is a protein comprising an amino acid sequence of SEQ ID NO: 2, wherein one or several amino acid residues are deleted, substituted, inserted and/or transposed and further compositions (medicaments) and fusion proteins comprising said proteins. The scope of the claims are not commensurate with the enablement provided by the disclosure with regard to the extremely large number of polypeptides i.e., any catalyst or any cleavage agent specifically cleaving one sugar chain or two or more sugar chains selected from the group consisting of hyaluronic acid, chondroitin sulfate A, C and D, said catalyst or cleavage agent is a protein comprising an amino acid sequence of SEQ ID NO: 2, wherein one or several amino acid residues are deleted, substituted, inserted and/or transposed and further compositions (medicaments) and fusion proteins comprising said proteins broadly encompassed by the claims. Since the amino acid sequence of a protein encoded by a polynucleotide determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires knowledge and guidance with regard to which amino acids in the protein's sequence and the respective codons in its polynucleotide, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the encoded proteins' structure relates to its function. However,

in this case the disclosure is limited to making and the use of an isolated catalyst or an isolated cleavage agent specifically cleaving one sugar chain or two or more sugar chains selected from the group consisting of hyaluronic acid, chondroitin sulfate A, C and D, said catalyst or cleavage agent is a protein comprising the amino acid sequence of SEQ ID NO: 2, composition (medicament) and fusion proteins comprising said protein, but provides no guidance with regard to the making of variants and mutants or with regard to other uses. In view of the great breadth of the claims, amount of experimentation required to make the claimed polypeptides, the lack of guidance, working examples, and unpredictability of the art in predicting function from a polypeptide primary structure (e.g., see Whisstock et al., Q Rev Biophys. 2003 Aug; 36(3): 307-340), the claimed invention would require undue experimentation. As such, the specification fails to teach one of ordinary skill how to use the full scope of the polypeptides encompassed by this claim.

While enzyme isolation techniques, recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications as required by the instant claims. The specific amino acid positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable (e.g., see Whisstock et al., Q Rev Biophys. 2003 Aug; 36(3): 307-340). In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish even further with additional modification, e.g. multiple substitutions or deletions or insertions or transpositions.

The specification does not support the broad scope of the claims i.e., any catalyst or any cleavage agent specifically cleaving one sugar chain or two or more sugar chains selected from the group consisting of hyaluronic acid, chondroitin sulfate A, B, C and D, said catalyst or cleavage agent is a protein comprising an amino acid sequence of SEQ ID NO: 2, wherein one or several amino acid residues are deleted, substituted, inserted and/or transposed and further compositions (medicaments) and fusion proteins comprising said proteins as claimed in claims 1-8, 16 and 17, because the specification does not establish: (A) regions of the protein/polynucleotide structure which may be modified without affecting the activity of catalyst or cleavage agent specifically cleaving one sugar chain or two or more sugar chains selected from the group consisting of hyaluronic acid, chondroitin sulfate A, C and D; (B) the general tolerance of the polypeptide and the polynucleotide encoding the activity of catalyst or cleavage agent specifically cleaving one sugar chain or two or more sugar chains selected from the group consisting of hyaluronic acid, chondroitin sulfate A, C and D to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any amino acid residue or the respective codon in the polynucleotide with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including polypeptides with an enormous number of modifications. The scope of the claim must bear a reasonable correlation with the scope of enablement (*In re Fisher*, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of polypeptides i.e.,

any catalyst or any cleavage agent specifically cleaving one sugar chain or two or more sugar chains selected from the group consisting of hyaluronic acid, chondroitin sulfate A, C and D, said catalyst or cleavage agent is a protein comprising an amino acid sequence of SEQ ID NO: 2, wherein one or several amino acid residues are deleted, substituted, inserted and/or transposed and further compositions (medicaments) and fusion proteins comprising said proteins broadly encompassed by the claims is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Written Description

Claims 1-8, 16 and 17 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1-8, 16 and 17 are directed to encompass any catalyst or any cleavage agent specifically cleaving one sugar chain or two or more sugar chains selected from the group consisting of hyaluronic acid, chondroitin sulfate A, C and D, said catalyst or cleavage agent is a protein comprising an amino acid sequence of SEQ ID NO: 2, wherein one or several amino acid residues are deleted, substituted, inserted and/or transposed and further compositions (medicaments) and fusion proteins comprising said proteins.

In *University of California v. Eli Lilly & Co.*, 43 USPQ2d 1938, the Court of Appeals for the Federal Circuit has held that "A written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials". As indicated in MPEP § 2163, the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of

species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show that Applicant was in possession of the claimed genus. In addition, MPEP § 2163 states that a representative number of species means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus.

Claims 1-8, 16 and 17, are rejected under this section 35 U.S.C. 112, because the claims as interpreted, are directed to encompass a genus of polypeptides i. e., any catalyst or any cleavage agent specifically cleaving one sugar chain or two or more sugar chains selected from the group consisting of hyaluronic acid, chondroitin sulfate A, C and D, said catalyst or cleavage agent is a protein comprising an amino acid sequence of SEQ ID NO: 2, wherein one or several amino acid residues are deleted, substituted, inserted and/or transposed and further compositions (medicaments) and fusion proteins comprising said proteins. No description of identifying characteristics of all of the sequences of an isolated polypeptide having an amino acid comprising the amino acid residues of SEQ ID NO: 2 wherein one or several amino acid residues are added, deleted, substituted, inserted and/or transposed and encoding a catalyst or cleavage agent specifically cleaving one sugar chain or two or more sugar chains selected from the group consisting of hyaluronic acid, chondroitin sulfate A, C and D has been provided by the applicants in the specification. No information, beyond the characterization of an isolated catalyst or an isolated cleavage agent specifically cleaving one sugar chain or two or more sugar chains selected from the group consisting of hyaluronic acid, chondroitin sulfate A, C and D, said catalyst or cleavage agent is a protein comprising the amino acid sequence of SEQ ID NO: 2, composition (medicament) and fusion protein comprising said protein has been provided by the applicants, which would indicate that they had possession of the claimed genus of the

polypeptides i.e., any catalyst or any cleavage agent specifically cleaving one sugar chain or two or more sugar chains selected from the group consisting of hyaluronic acid, chondroitin sulfate A, C and D, said catalyst or cleavage agent is a protein comprising an amino acid sequence of SEQ ID NO: 2, wherein one or several amino acid residues are deleted, substituted, inserted and/or transposed and further compositions (medicaments) and fusion proteins comprising said proteins. Therefore, one skilled in the art cannot reasonably conclude that applicant had possession of the claimed invention at the time the instant application was filed.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Claim Rejections 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-8 are rejected under 35 U.S.C. 102(b) as being anticipated by Stern et al[1]., (WO 99/29841, publication date 06/17/1999 in IDS) or Stern et al[2]., (US Patent No.: 6,123,938, 09/26/2000) when given the broadest interpretation. Claims 1-8 are directed to any catalyst or any cleavage agent specifically cleaving one sugar chain or two or more sugar chains selected from the group consisting of hyaluronic acid, chondroitin sulfate A, C and D, said catalyst or cleavage agent is a protein comprising an amino acid sequence of SEQ ID NO: 2, wherein one or several amino acid residues are deleted, substituted, inserted and/or transposed and further

compositions (medicaments) comprising said proteins. Note, claims 7 and 8 are also included in the instant rejection, as said claims are directed to intended use i.e., site of delivery of the product and therefore patentable weight is not given to limitations in the claims such as "... living body tissue is nucleus pulposus" (as in claim 7) and "... agent for treating disc herniation" (as in claim 8). Stern et al[1]., or Stern et al[2]., disclose isolation of a human polypeptide annotated as hyaluronidase enzyme having 100% sequence identity to SEQ ID NO: 2 of the instant application. Said reference also discloses hyaluronidases are a group of enzymes that degrade hyaluronan and chondroitin sulfates (chondroitinase activity), said hyaluronidase as a therapeutic agent, assays for identification of biologically active hyaluronidase and characterization of said hyaluronidase (Stern et al[1]: page 1, lines 14-16; page 2, line 21-23; page 5, lines 4-6; page 26, lines 19-28; page 27, lines 15-19; page 37, Example 4; page 40, Claim 18). Although said reference does not explicitly disclose said polypeptide not capable of cleaving derman sulfate, keratin sulfate and chondroitin having an average molecular weight of 7,000 (as in claims 2, 4 and 6 of the instant application), examiner takes the position that such properties would be inherent to the enzymatic activity of the disclosed polypeptide in the reference of Stern et al[1]., or Stern et al[2]., by virtue of 100% sequence identity to SEQ ID NO: 2 of the instant invention, unless applicants' provide evidence to the contrary. Therefore the references of Stern et al[1]., (WO 99/29841, publication date 06/17/1999 in IDS) or Stern et al[2]., (US Patent No.: 6,123,938, 09/26/2000) anticipate claims 1-8 of the present invention.

Claim Rejections 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Stern et al[1]., (WO 99/29841, publication date 06/17/1999 in IDS) or Stern et al[2]., (US Patent No.: 6,123,938, 09/26/2000) and in view of Nohara et al., (US Patent No.: 6,063,378, 05/16/2000). The teachings of Stern et al[1]., or Stern et al[2]., are described above (see 102 (b) rejection). Although Stern et al[1]., or Stern et al[2]., teach the isolation of a human polypeptide annotated as hyaluronidase enzyme having 100% sequence identity to SEQ ID NO: 2 of the instant application and said reference also teaches hyaluronidases are a group of enzymes that degrade hyaluronan and chondroitin sulfates (chondroitinase activity) and use as a therapeutic agent, said references are silent regarding said therapeutic agent use as a medicament for cleaving hyaluronic acid and chondroitin sulfates present in a living body tissue such as nucleus pulposus and for treating disc herniation. Nohara et al., teach the use of chondroitinase ABC, a glycosaminoglycan (hyaluronic acid and chondroitin sulfates) degrading enzyme and as a medicament for the treatment of herniated inter-vertebral disc (inter-vertebral disc dissolution treating method) in living tissues such as nucleus pulposus (Abstract section, columns 1-2; column 16, claims 1-15; and entire document). It would have been obvious to a person of ordinary skill in the art to combine the teachings of Stern et al[1]., or Stern et al[2]., and Nohara et al., to use a catalyst or a cleavage agent that specifically cleaves one sugar chain or two or more sugar chains selected from the group

consisting of hyaluronic acid, chondroitin sulfates, said catalyst or cleavage agent is a protein comprising an amino acid sequence of SEQ ID NO: 2 as a therapeutic agent/medicament for the treatment of herniated inter-vertebral disc (inter-vertebral disc dissolution treating method) in living tissues such as nucleus pulposus. Motivation to do so derives from the pharmaceutical importance of chondroitinases that are shown to be superior to other proteolytic enzymes used in disc dissolution treating method, because proteolytic enzymes are shown to have several disadvantages such as causing neuronal paralysis and onset of allergy (Nohara et al., column 1, line 55-66). The expectation of success is high, because Stern et al[1]., or Stern et al[2]., and Nohara et al., teach pharmaceutical compositions comprising human derived chondroitinases and therapeutic compositions comprising said chondroitinases in pharmaceutical carriers, method of use and indications of use in the treatment of herniated inter-vertebral disc (inter-vertebral disc dissolution treating method) in living tissues such as nucleus pulposus. Therefore, claims 1-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Stern et al[1]., (WO 99/29841, publication date 06/17/1999 in IDS) or Stern et al[2]., (US Patent No.: 6,123,938, 09/26/2000) and in view of Nohara et al., (US Patent No.: 6,063,378, 05/16/2000).

Claims 16 and 17 are rejected under 35 U.S.C. 103(a) as being unpatentable over the combination of Stern et al[1]., (1999) or Stern et al[2]., (2000) and Nohara et al., (2000) and further in view of Berlowitz-Tarrant et al., (WO 95/13091, publication date 05/18/1995). The combination of Stern et al[1]., (1999) or Stern et al[2]., (2000) and Nohara et al., (2000) is described above. Said combination does not specifically teach chondroitinases as a fusion protein. However, pharmaceutical compositions comprising chondroitinases as fusion proteins were well known in the art (Berlowitz-Tarrant et al., 1995). Berlowitz-Tarrant et al., teach the use of extra-

cellular matrix altering enzymes such as prteoglycanase/chondroitinase (Abstract section, page 3, lines 17-25; page 7, lines 22-29; page 9, line 36 to page 10, line 23) as a chimeric protein comprising additional moiety such as fibronectin that binds to a component of extra-cellular matrix for better absorption and localization of the chimeric molecule in a treatment site, said fusion protein can be generated as recombinant fusion gene or by chemical cross-linking. It would have been obvious to a person of ordinary skill in the art to combine the teachings of Stern et al[1]., or Stern et al[2]., Nohara et al., and Berlowitz-Tarrant et al., to generate a fusion protein i.e., a catalyst or a cleavage agent specifically cleaving one sugar chain or two or more sugar chains selected from the group consisting of hyaluronic acid, chondroitin sulfate A, C and D, said catalyst or cleavage agent is a protein comprising an amino acid sequence of SEQ ID NO: 2 and further comprising an additional protein of interest as a fusion protein depending on the experimental/therapeutic need. Motivation to do so derives from the commercial and pharmaceutical importance of chondroitinases that are shown to be superior to other proteolytic enzymes for use in disc dissolution treating method (Stern et al[1]., or Stern et al[2]., and Nohara et al.,). The expectation of success is high, because pharmaceutical compositions comprising chondroitinases as fusion proteins were well known in the art (Berlowitz-Tarrant et al., 1995) and furthermore fusion proteins enable better localization and targeting to the treatment site of pharmaceutical compositions comprising chondroitinases. Therefore, claims 16 and 17 are rejected under 35 U.S.C. 103(a) as being unpatentable over the combination of Stern et al[1]., (1999) or Stern et al[2]., (2000) and Nohara et al., (2000) and further in view of Berlowitz-Tarrant et al., (WO 95/13091, publication date 05/18/1995).

The above references render claims 1-8, 16 and 17 *prima facie* obvious to one of ordinary skill in the art.

Allowable Subject Matter/Conclusion

None of the claims are allowable.

Final Comments

To insure that each document is properly filed in the electronic file wrapper, it is requested that each of amendments to the specification, amendments to the claims, Applicants' remarks, requests for extension of time, and any other distinct papers be submitted on separate pages.

It is also requested that Applicants identify support, within the original application, for any amendments to the claims and specification.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ganapathirama Raghu whose telephone number is 571-272-4533. The examiner can normally be reached between 8 am-4: 30 pm EST. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Nashaat Nashed can be reached on 571-272-0934. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300 for regular communications and for After Final communications. Any inquiry of a general nature or relating to the status of the application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Ganapathirama Raghu/
Patent Examiner
Art Unit 1652
Apr. 29, 2008.